A Facile and Unexpected Synthesis of 2,3-Bis-(*N*-alkylanilino)propenals and 1,1-Bis(*p*-alkylaminoaryl)propan-2-ones *via* Oxidative Aminomercuriation of Prop-2-ynol

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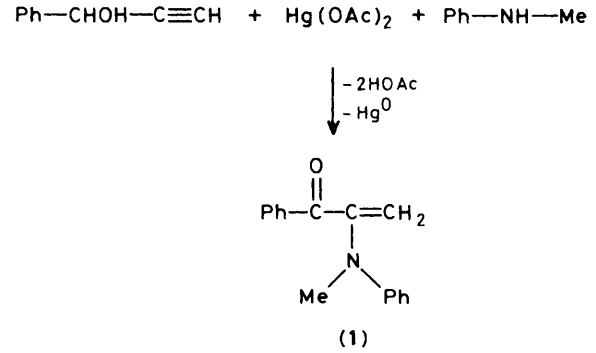
The course of the oxidative aminomercuriation of prop-2-ynol using secondary aromatic amines depends on the acidity of the reaction medium in such a way that the process may be exclusively directed towards the synthesis of 2,3-bis(*N*-alkylanilino)propenals (**2**) or 1,1-bis-(*p*-alkylaminoaryl)propan-2-ones (**3**), respectively.

We have recently employed the oxidative aminomercuriation of prop-2-ynyl alcohols using *primary* amines for the synthesis of α-di-imines and related compounds,[1] and several heterocyclic systems.[2] The isolation of the cross-linked enaminone (**1**) using *N*-methylaniline as nucleophile (Scheme 1)[1,3] allowed us not only to gain some insight into the mechanism of the process, but it also demonstrated the ability of *secondary* amines to participate in oxidative aminomercuriation of prop-2-ynyl alcohols.

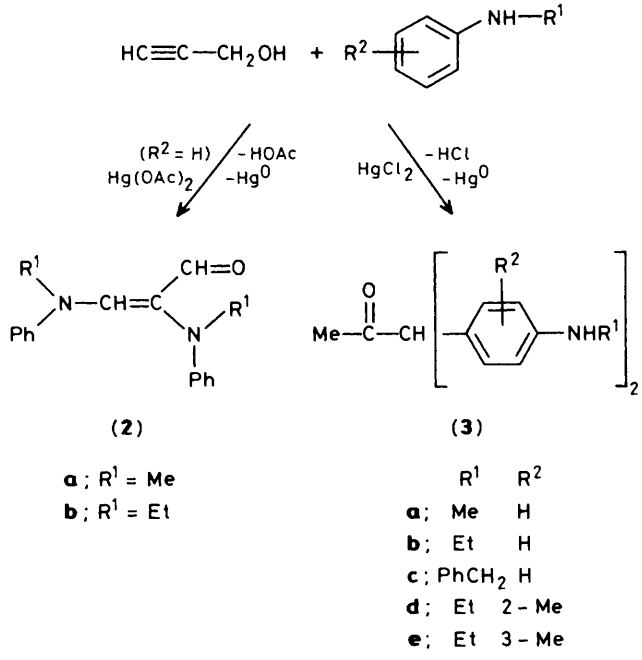
We now report the preliminary synthetic results of the reactions of prop-2-ynol, secondary aromatic amines, and a mercury(II) salt. Surprisingly, the products markedly depend on the nature of the mercury(II) salt employed, in contrast with the processes involving primary amines. Thus, using



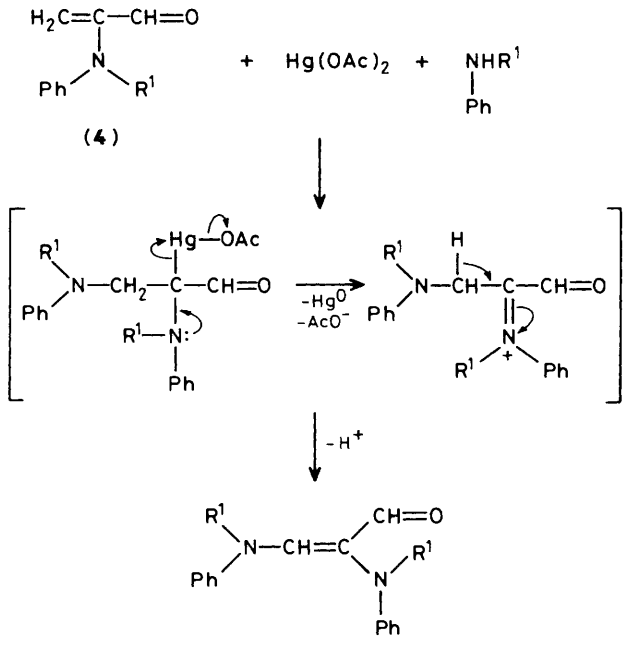
Scheme 1

mercury(II) acetate a crude reaction mixture, whose ^{1}H n.m.r. spectrum displayed a sharp aldehydic signal, was obtained; from the crude mixture we were able to isolate the highly functionalized 2,3-bis(*N*-alkylanilino)propenals (**2**). In contrast, when mercury(II) chloride was used a more complex mixture, which showed no aldehydic ^{1}H n.m.r. signal, resulted and the corresponding 1,1-bis(*p*-alkylaminoaryl)propan-2-one (**3**) could be isolated (Scheme 2).† Compounds of type (**3**) have been previously prepared[4] as analogues of amphenone B[5] and possess a high degree of adrenal inhibitory activity.[4a]

Further investigations showed that the acidity of the reaction medium plays a decisive role in the course of the process, allowing it to be directed in a single and predetermined sense. Thus, the use of mercury(II) acetate and a slight excess of triethylamine led exclusively to the diaminoacroleins (**2**),‡ while mercury(II) chloride and a catalytic amount of trifluoroacetic acid yielded only the amphenone analogues (**3**).§



Scheme 2



Scheme 3

The formation of compounds (**2**) and (**3**) can be understood in terms of two initial catalytic and oxidative steps[1] leading to the 2-(*N*-alkylanilino)propenal (**4**) analogous to (**1**). However, 2,3-diaminopropenals (**2**) are more highly oxidized materials than the intermediates (**4**) and, so, a further aminomercuriation¶ and oxidative β-elimination[7] sequence can be envisaged (Scheme 3).

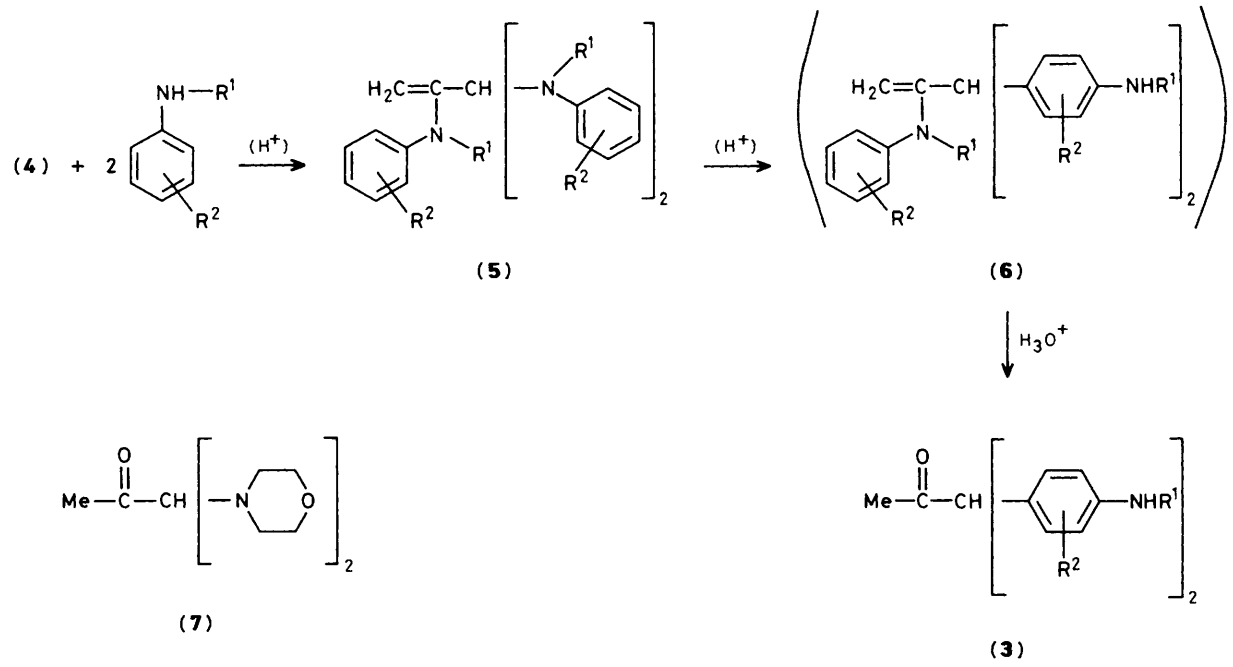
1,1-Bis(*p*-alkylaminoaryl)propan-2-ones (**3**) may originate by a double amination of (**4**), followed by acid-catalysed

† Satisfactory elemental (C, H, N) analyses were obtained for compounds (**2**) and (**3**).

‡ In a typical run, a mixture of prop-2-ynol (10 mmol), mercury(II) acetate (20 mmol), an *N*-alkylaniline (50 mmol), triethylamine (40 ml), and dichloromethane (30 ml) was stirred overnight (0—25 °C). After filtering off the partially precipitated metallic mercury, a solution of sodium borohydride (20 − *n* mmol; *n* = mmol of precipitated mercury) in 3 M aqueous potassium hydroxide (20 ml) was added to reduce the remaining mercury(II) species. After 2—3 h, the resulting mixture was filtered, extracted with dichloromethane, and concentrated (15 and 0.05 Torr, successively). The crude product was chromatographed on silica gel, using ether as eluant, to yield (35—54%) the diaminoaldehyde (**2**) as a very viscous red oil [*e.g.* (**2a**), i.r. (film) ν(C=O) 1670 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$) 3.1 (s, 3H), 3.4 (s, 3H), 6.5—7.5 (m, 11H), and 9.15 (s, 1H); ^{13}C n.m.r. δ ($CDCl_3$) 36.3 (q), 37.3 (q), 110.8 (d), 115.4 (d), 119.5 (d), 122.1 (long range d), 123.9 (d), 127.4 (d), 127.7 (d), 145.3 (s), 146.9 (s), 149.5 (d), and 187.1 (d); *m/z* 266 (M^+)]. These spectroscopic data are consistent with the presence of a single stereoisomer, probably the (*E*)-form for steric reasons.

§ 1,1-Bis(*p*-alkylaminoaryl)propan-2-ones (**3**) were prepared by a method analogous to that for (**2**) as amorphous, non-recrystallizable solids by refluxing overnight a stirred mixture of prop-2-ynol (20 mmol), mercury(II) chloride (20 mmol), an *N*-alkylarylamine (80 mmol), trifluoroacetic acid (4 mmol), and tetrahydrofuran (30 ml). Chromatography on silica gel using first cyclohexane–ether (1 : 1) as eluant for removing impurities, and then acetone, gave (41—61%) compound (**3**) [*e.g.* (**3a**), i.r. (film) ν(C=O) 1720, ν(N–H) 3440 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$) 2.25 (s, 3H), 2.85 (s, 6H), 3.45 (s, 2NH), 4.85 (s, 1H), 6.5 (d, 4H), and 7.0 (d, 4H); ^{13}C n.m.r. δ ($CDCl_3$) 27.8 (q), 28.9 (q), 62.1 (d), 111.0 (d), 126.1 (s), 128.1 (d), 146.8 (s), and 192.8 (s); *m/z* 268 (M^+)].

¶ A closely related aminomercuriation of α,β-unsaturated esters has previously been described.[6]



Scheme 4

rearrangement of the aminal (**5**)[8] and hydrolysis of the enamine (**6**) in the subsequent aqueous work-up (Scheme 4).

In order to ascertain the participation of the aminal intermediates of type (**5**) we have carried out the reaction of prop-2-ynol, mercury(II) chloride, and morpholine (molar ratio 1:1:4) in the presence of an excess of potassium carbonate in tetrahydrofuran (THF), and found that 1,1-dimorpholinopropan-2-one (**7**) was formed in high yield.

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References

1 J. Barluenga, F. Aznar, and R. Liz, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1093.

2 (a) J. Barluenga, F. Aznar, R. Liz, and M.-P. Cabal, *Synthesis*, 1985, 313; (b) J. Barluenga, F. Aznar, R. Liz, M.-P. Cabal, F. H. Cano, and C. Foces-Foces, *Chem. Ber.*, 1986, **119**, 887.

3 R. Liz, Ph. D. Thesis, University of Oviedo, 1981.

4 (a) J. B. Wright and E. S. Gutsell, *J. Am. Chem. Soc.*, 1959, **81**, 5193; (b) J. B. Wright, U.S. Pat. 2,881,175 (April 7, 1959) (*Chem. Abstr.*, 1960, **54**, 1453a); (c) J. B. Wright, U.S. Pat. 2,993,927 (July 25, 1961) (*Chem. Abstr.*, 1962, **56**, 3410d).

5 (a) T. Kido, M. Arakawa, and T. Kimura, *J. Biol. Chem.*, 1979, **254**, 8377; (b) J. Klimek, A. P. Schaap, and T. Kimura, *Biochim. Biophys. Acta*, 1983, **752**, 127.

6 J. Barluenga, J. Villamaña, and M. Yus, *Synthesis*, 1981, 375.

7 J. Barluenga, F. Aznar, R. Liz, and R. Rodes, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2732.

8 E. C. Wagner, *J. Org. Chem.*, 1954, **19**, 1862; A. M. Bayón, Ph.D. Thesis, University of Oviedo, 1984.